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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,124	01/28/2004	Jane Hirsh	CP 108	2103

23579 7590 04/02/2008

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EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
04/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,124	HIRSH ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 - 4, 8, 11, 12, 15 - 29* is/are pending in the application.

4a) Of the above claim(s) *11,16,23,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 - 4, 8, 12, 15, 17 - 24, 27 - 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/7/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed February 1, 2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Comments and Notes

It is noted that Applicant did not affirm the election made in Office Action mailed October 1, 2007 nor provide a summary of the interview that took place on August 27, 2007.

Election/Restrictions

1. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and therefore made FINAL.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 21, 22 and 24 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Due to the amendments to the claims and clarification provided by Applicant, this rejection is WITHDRAWN.

4. Claim 18 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Due to the amendments to the claims, this rejection is WITHDRAWN.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1 – 10, 12 – 15, 17, 18 and 27 – 28 were rejected under 35 U.S.C. 103(a) as being unpatentable over Eichman (US Patent 5,980,882). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 1, 2007 and those set forth below. Due to the amendments to the claims, this rejection is now applied to claims 1 – 4, 8, 11, 15, 17, 18 and 27 – 29.

Applicant traverses this rejection on the basis that Eichman does not teach or suggest a composition that provides both a delayed and extended release of milnacipran. Also, the decreased incidence of side effects associated with the delayed and extended release profile is not discussed by Eichman.

This argument is not found persuasive. The definitions of modified, delayed, extended, and pulsatile release profiles provided by Applicant on p 9, ln 24 – p 10, ln 9 of the specification are extremely broad. Any oral composition of milnacipran would have a "delayed release" as the drug release occurs at a later time after administration when compared to intravenous administration. Eichman does suggest the inclusion of an enteric coating layer. Such a layer is designed to resist dissolution in the acidic environment in the stomach so that the release and absorption of the drug is delayed until the composition enters the small intestine, resulting in a delayed release of milnacipran even in comparison to other oral dosage forms. As the complexation of the drug with ion-resin leads to slower dissolution, it therefore provides an extended release as the solid dosage form provides at least a twofold reduction in the dosing frequency as compared to a intravenous solution dosage form.

The diminished incidence or reduced intensity of the side effects is necessarily provided by the altered release profile of the milnacipran and so while the cited prior art does not explicitly teach a diminished incidence or reduced intensity of side effects, this property is inherent to the composition that is described by the prior art.

It is also unclear what Applicant means on p 12 by "it would not be obvious to replace the enteric coating with the delayed and extended release coatings of the claimed compositions". In claim 1, no coatings are described for the composition but rather recite a composition comprised of milnacipran complexed with an ion-exchange resin. A coating step with one or more polymers is required on claim 28 but no limitations on the types of polymers or release profiles they impart are present in the claim. While claim 8 does require a coating layer, it is an enteric coating that is described in the prior art.

7. Claims 1 – 10, 12 – 15, 17, 18, 21, 22, 24, 27 and 28 were rejected under 35 U.S.C. 103(a) as being unpatentable over Eichman in view of Paillard et al.
This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 1, 2007 and those set forth herein. Due to the amendments to the claims, this rejection is now applied to claims 1 – 4, 8, 11, 12, 15, 17, 18, 21, 22, 24 and 27 – 29.

Applicant argues that Eichman does not teach a combination of coatings or a combination of delayed and extended release. Applicant argues that Paillard describes a prolonged release of milnacipran with only one type of microgranule per formulation.

The polymers described are extended or sustained release polymers, and not delayed release polymers. Therefore the composition disclosed by Paillard provides extended, but not a mixture of delayed and extended release composition. Additionally, there is no teaching in Paillard of a combination of release profiles. Paillard also does not suggest diminished incidence or reduced intensity of either locally or centrally mediated side effects of the milnacipran.

This is not persuasive because Paillard was relied upon for the stereochemical makeup of the milnacipran and that racemic milnacipran is suitable for use in a non-immediate release formulation. The claims of the instant application do not require that different populations microparticle provide each release profile. As discussed above, the ion-resin complexed milnacipran provides a delayed release and extended release formulation and therefore the two different release profiles are provided by one type of microgranule. As such, a combination of delayed and extended release coatings need not be present in the composition to meet the definitions of these terms as provided by Applicant.

8. Claims 19 and 20 were rejected under 35 U.S.C. 103(a) as being unpatentable over Eichman and Paillard in view of Kranzler et al. This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 1, 2007 and those set forth herein.

Applicant traverses this argument by saying that while Kranzler et al. does disclose a combination of milnacipran and other active compounds such as analgesics,

Kranzler does not suggest a formulation that provided both a delayed and extended release and that none of these references suggest reduces in the frequency or diminishes the intensity of locally and centrally mediated side effects.

As discussed in more detail above, Eichman and Paillard disclose a composition of milnacipran, that be in a racemic form, complexed with an ion-exchange resin that can be optionally coated with an enteric coating. Even without the enteric coating, the ion-exchange resin complex of milnacipran does meet the broad definitions of both delayed and extended release of the active ingredient. As the requirements for the release profile of the claim are met by the cited prior art, the diminished incidence or reduced intensity of side effects necessarily provides the alterations in the side effects such as nausea. Therefore Applicants arguments are not persuasive and this rejection is maintained.

Double Patenting

Applicant has argued that the Examiner was legally incorrect in relying upon the disclosure of the patents as prior art when making a double patenting rejection. The disclosure of the patent or application may be relied upon only to define the claim (**MPEP 1504.06**). It is noted that the disclosures of the patents were used as a secondary reference, in view of the claims of the US patent/application, which is allowed. For the primary reference in the double patenting rejection, only the claims were relied upon. However, when used as evidence to support a double patenting

rejection, the entire disclosure of the document, whether it is a patent, pre-grant publication or non-patent literature, can be used. In the rejections discussed below, the Eichman and Paillard patents are being used as evidence to support the rejection and therefore their entire disclosures can be used and reference to particular claims is not required. The disclosure of the copending applications involved in the rejections can only to be used to define the claim.

9. Claim 28 was provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 27 of copending Application No. 11/192697 in view of Eichman and Paillard

In addition to traversal on the basis of improper use of the disclosure of Eichman and Paillard discussed above, this rejection is also traversed on the grounds that the claims of '697 require pulsatile release while the claims of the instant application require a delayed and extended release of the milnacipran. Applicant also traverses this rejection on the basis that neither Eichman nor Paillard disclose or suggest any change in the side effects associated with the composition.

The definition of pulsatile cited on p 21 of the remarks comes from the instant application but in defining this term, the specification of '697 should be consulted. Using the specification to define a term in the claims is allowed for the patent or copending Application involved in the double patenting rejection. Pulsatile is defined on p 9, ln 5 – 11 of the specification of '697, and is characterized as having a time period of no release or reduced release followed by rapid drug release and is defined relation to a

conventional dosage form such as a solution. The reduced release portion of the definition meets the definition of delayed release presented in the instant application. There is no indication that the rapid drug release cannot occur over an extended period of time and only faster than the release rate during the initial period. Because of the broad definitions of the various release profiles, pulsatile release and a delayed and extended release profile are not patentably distinct. The decreased incidence of side effects is inherent do the altered release profile of the milnacipran.

Therefore this provisional rejection is MAINTAINED.

10. Claims 1, 8, 13, 15, 20, 21, 22 and 24 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 9, 12, and 16 – 18 of copending Application No. 10/690872 in view of Eichman and Paillard.

In addition to traversal on the basis of improper use of the disclosure of Eichman and Paillard discussed above, this rejection is also traversed on the grounds that the pulsatile release profile of the claims of '872 is patentably distinct from the delayed and extended release of the claims of the instant application. Applicant also traverses on the basis that neither Eichman nor Paillard disclose or suggest any change in the side effects associated with the composition.

Pulsatile is defined on p 16, ln 4 – 9 of the specification of '872, and is characterized as having a time period of no release or reduced release followed by rapid drug release and is defined relation to a conventional dosage form such as a

solution. The reduced release portion of the definition meets the definition of delayed release presented in the instant application. There is no indication that the rapid drug release cannot occur over an extended period of time and is faster than the release rate during the initial period. The claims of the instant application require the milnacipran be complexed with an ion-exchange resin and Eichman teaches that one formulation that provides a release pattern that matches the definition of pulsatile in '872 and delayed and extended in the instant application is by complexation of the drug with an ion-exchange resin. Because of the broad definitions of the various release profiles, pulsatile release and a delayed and extended release profile are not patentably distinct. The decreased incidence of side effects is inherent do the altered release profile of the milnacipran.

Therefore this provisional rejection is MAINTAINED.

11. Claim 27 was provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 24 of copending Application No. 10/690947 in view of Eichman and Paillard (the serial number for this rejection, cited in paragraph 2 on p 23 was incorrect; the serial number indicated above is the correct serial number).

In addition to traversal on the basis of improper use the disclosure of Eichman and Paillard, this rejection is also traversed on the grounds that the claim of the instant application requires complexation of the milnacipran to an ion-exchange resin that is not required in claim 24 of '947.

The disclosure of Eichman and Paillard, used as secondary references whose entire disclosures may be relied upon, teaches that complexation of milnacipran with an ion-exchange resin is a formulation capable of delivering the delayed and extended release profiles that are required in the claims of both the instant and copending applications.

Therefore this provisional double patenting rejection is MAINTAINED.

12. Claims 1, 8, 15, 17, 18 and 20 – 22 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 5, 9, 12 and 15 – 17 of copending Application No. 10/691936 in view of Eichman and Paillard.

In addition to traversal on the basis of improper use of the disclosure of Eichman and Paillard, this rejection is also traversed on the grounds that complexation with an ion-exchange resin and coating the resulting particles are not obvious variants of the claims of the copending application.

The disclosure of Eichman and Paillard, used as secondary references whose entire disclosures may be relied upon, teaches that complexation of milnacipran with an ion-exchange resin is a formulation capable of delivering the delayed and extended release profiles that are required in the claims of both the instant and copending application.

Therefore this provisional double patenting rejection is MAINTAINED.

13. Claims 1, 8, 10, 15, 20, 21 and 24 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 9, 11, 14 – 16, 18 and 19 of copending Application No. 11/192885 in view of Eichman and Paillard.

In addition to traversal on the basis of improper use of the disclosure of Eichman and Paillard, this rejection is also traversed on the grounds that complexation with an ion-exchange resin and coating the resulting particles are not obvious variants of the claims of the copending application.

The disclosure of Eichman and Paillard, used as secondary references whose entire disclosures may be relied upon, teaches that complexation of milnacipran with an ion-exchange resin is a formulation capable of delivering the delayed and extended release profiles that are required in the claims of both the instant and copending application.

Therefore this provisional double patenting rejection is MAINTAINED.

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW